Proceedings of the NIEHS Strategic Planning Forum

October 17-18, 2005

Introduction

The NIEHS Strategic Plan 2006 Process

The NIEHS is formulating a new strategic plan to guide its activities over the next five-year period. With the intent that the process be as inclusive and transparent as possible, input has been solicited from a wide variety of sources within the scientific community, the institute itself, and the general public.

The process officially began in June, 2005, with the publication of a notice in the Federal Register requesting public comment and nominations for participation in the Strategic Planning Forum. More than 400 responses were received, via both a website designed for that purpose and direct email, mail and fax submissions. Responses were received from scientists, clinicians, educators, advocacy group members, industry representatives, and other stakeholders. That input helped to shape the agenda, invitation list, and goals and objectives of the Forum, along with the guidance of a 20-member Steering Committee chaired by Dr. Samuel H. Wilson, Deputy Director of the NIEHS.

This document, *Proceedings of the NIEHS Strategic Planning Forum*, will be distributed for comment, which will contribute to the content of the final draft of the *NIEHS Strategic Plan*, due to be completed and presented to the NIEHS Council in February, 2006.

Proceedings of the NIEHS Strategic Planning Forum

October 17-18, 2005

The NIEHS Strategic Planning Forum

More than 100 participants (attendees list is attached) representing a wide variety of disciplines and interests attended the NIEHS Strategic Planning Forum, held October 17-18, 2005 at the Sheraton Chapel Hill Hotel, Chapel Hill, North Carolina. The Forum was co-chaired by Dr. Frederica Perera of Columbia University and Dr. Gerald Wogan of the Massachusetts Institute of Technology, and was organized by Dr. Sheila Newton, Director, Office of Science Policy and Planning, NIEHS.

The Forum was designed to be an intensive, comprehensive consideration of the challenges and opportunities facing the institute in the coming years, and to generate specific recommendations for future basic and clinical research priorities. Three in-depth, two-hour breakout cycles were the central activities of the meeting, each consisting of eight discussion groups with nine to twelve participants carefully composed to include discussants from the various represented disciplines and backgrounds. In each cycle, four groups considered one of the six overarching topics pre-chosen for focused discussion. The flow of discussion for each topic was further directed by several questions designed to elicit consideration of specific issues. Following each cycle, attendees re-convened in plenary session, during which the discussion leaders from each of the groups described the key points that emerged from their deliberations, supported by brief PowerPoint presentations prepared immediately following the discussion.

In his opening remarks, NIEHS Director Dr. David Schwartz set the tone for the discussions to follow, asking Forum participants to concentrate on three major goals:

> *"First, it is essential that we focus on the priorities and the opportunities in the field. What are the major challenges? What are the big questions that we should be addressing? And how should we prioritize those questions?*
>
> *Second, we need to formulate a plan and focus on the very best science—science that will have the largest impact on human health and disease. If we can focus on the scientific efforts relevant to human health and disease, I can assure you that five to ten years from now, we will be able to show some very substantial successes in this area.*
>
> *Third, we need to prepare for the future. We need to think about what our deficiencies are in the work force as it relates to environmental health sciences, and what programs we should develop that will attract the best and brightest individuals to NIEHS and to our field, so that we can have the biggest impact on human health and disease.*
>
> *The goal of this conference is to identify the goals and objectives that will guide our growth over the next five years. What we're looking for are new ideas and new challenges that can help move our institute forward in a powerful way, and ultimately have a profound effect on human health and disease.*

The balance of this report will summarize the important points that emerged during the discussions among the groups that addressed each of the six pre-assigned topics. Special attention will be paid to ideas that rose to the level of consensus among the groups, as this suggests consensus within the larger community of stakeholders concerned with the future direction of NIEHS. Points that arose in more than one group will also be presented, as will concepts of interest that were mentioned in one group only, and other salient unresolved issues or alternative interpretations.

Proceedings of the NIEHS Strategic Planning Forum

October 17-18, 2005

Topic I:

Using Environmental Sciences and Environmental Exposures to Understand Human Biology

- What will be the most critical biological systems and pathways through which environmental agents exert their effects on human systems? Which have the broadest impact on important disease processes?
- What are the biological processes about which we lack information that may be critical for new understanding of how environmental agents exert their effects on human systems? Which of these will represent areas in which the likelihood of uncovering important new mechanisms of environmental effects is greatest? How can different approaches work together to determine human disease risk from environmental exposures to these processes?
- Looking forward, what are the most exciting new frontiers of environmental health science and human biology? What are the innovative approaches? How can we develop and foster the best science?
- What is the goal of this approach?

A	B	C	D
John Hildebrandt	**Mike Gallo**	**David Eaton**	**Jim Swenberg**
Vas Aposhian	Jim Bus	Trevor Archer	Steve Akiyama
Bill Farland	Kathleen Dixon	Joe Graziano	Chris Bradfield
John Groopman	Traci Hall	Carol Henry	Robert Floyd
Tom Kunkel	Randy Jirtle	Michelle Hooth	Bruce Hammock
Lee Newman	Cynthia McMurray	Bruce Lanphear	Howard Hu
Ken Ramos	Regina Santella	Irva Hertz-Picciotto	Ken Korach
Carrie Redlich	Martyn Smith	Jim Popp	Stephanie London
Ellen Silbergeld	Jack Taylor	Steve Safe	Ivan Rusyn
David Wheeler		Marsha Wills-Karp	Hal Zenick
Mary Wolfe, writer	Kim McAllister, writer	Pat Mastin, writer	Bill Jirles, writer
Janet Guthrie, recorder	Brenda Weis, recorder	Jerry Phelps, recorder	Stephanie Holmgren, recorder

Although specific language and ideas varied somewhat, several common themes arose among the groups.

Systems Approach/Data Integration/Multidisciplinary Research

“An overriding issue that continued to come up throughout our discussions was the necessity of having a multidisciplinary, integrative approach to all of our research projects.”

One group characterized this concept as a dichotomous need to integrate the biology with the agent (i.e., understanding basic biology to understand responses to environmental agents) and to integrate the agent with the biology (i.e., relating the effects of environmental agents with critical biological pathways). This **systems-oriented approach** would integrate data from all levels of investigation to promote comprehensive understanding of the relationship between environmental agents and the underlying biology, including:

- Subcellular: inorganic ion interactions, protein structure, computational approaches, bioorganic chemistry, identification/characterization of molecular targets
- Cell: cell signaling, genome stability (DNA damage and repair), epigenetics, protein stability (synthesis, regulation), proliferation, cell death (apoptosis), differentiation/dedifferentiation
- Tissue: cell metastasis, hyperplasia, cell matrix, immune response, necrosis
- Organ: angiogenesis, carcinogenesis
- Person
- Population

To accomplish this ambitious vision, new tools and new infrastructure will be required. All groups discussed the need for **improved bioinformatics** to help extract knowledge from the huge amounts of data being generated now and in the future, and to integrate that knowledge across environment, biology, and disease to most effectively ameliorate public health. One group characterized this as a “need to link omics to physiology.”

The need for new and better incentives for **cross-disciplinary research** was also a prominent theme. One group recognized that NIEHS faces a dilemma in this mission: the institute should build an infrastructure for complex, integrative, **large-scale science**, which requires experienced scientists, but should also incorporate the innovative solutions offered by high-risk science, which would likely involve younger scientists, and raises issues of training and limited funding. Another group’s ideas to encourage cross-disciplinary, integrative research included:

- Cross-agency approaches
- Clinical trainees
- Joint funding efforts to experts in EHS and in disease/clinical aspects
- Need for an environmental health IRG

Another panel urged that NIEHS consider funding a research consortium dedicated to elucidating biological mechanisms for specific diseases, and that the institute should focus on new prospective human studies, entering that information into a central repository, including biosamples, that would be widely accessible. The same group recommended the creation of libraries across model systems (e.g., RNAi, KOs), with associated bioinformatics tools, as well as libraries devoted to the study of gene-gene interactions and gene-protein interactions.

Characterizing Exposures in Human Populations

The need for improved and expanded methods of characterizing exposures in human populations was another theme touched upon in all groups. This took the form of several common suggestions in specific areas.

An ongoing need for improvement in **dose-response** methodologies was identified, particularly in **extrapolation** of results from high-dose experiments to low-dose effects, and the ability to accurately measure and characterize **low-dose responses** (including hormesis), **cumulative exposures**, **chronic exposures**, **reduced exposures** (through experimental trials and study of natural experiments), **amplified** exposures (agents whose biological effects are amplified within the system), and **mixtures and complex exposures**.

Among the many ideas discussed to foster needed exposure assessment improvements, **biomarkers** was the most prominent. One group suggested the establishment of Centers for Excellence for Biomarker Development. The need for more validated biomarkers touched upon several areas of research, including susceptibility (individual and population; predictive), persistent exposures (quantitative biomarkers), biomarkers of exposure within specific developmental periods (e.g., the young and the aged), and biomarkers of changes or effects within physiologic subsystems reflective of gene-environment interactions.

All groups also touched upon the continuing need for improved **animal models**. More animal models of **human disease** were suggested, including more use of **"humanized" mouse models** to enhance understanding of exposures and disease. One group called for more use of **older animals**, to model the long-term effects of exposure and aging. Similarly, a group discussed the need for **broader mouse models**, in that a wider diversity of genetic strains would enhance understanding of susceptibility and dose-response, helping to identify key "master control systems," and would result in improved ability to extrapolate and translate findings to humans. Another group suggested additional and improved use of all animal models, *in vivo* and *in vitro*, to study the role of **epigenetics**. It was also mentioned that there is a need to improve **sharing of transgenic animals**, to maximize the use of resources and avoid redundant work developing similar or identical model strains. Improved ability to conduct **cross-species comparisons** was also recommended.

Important Biological Systems, Pathways, and Processes

Commonalities among two or more of the groups emerged in their answers to the questions asked regarding this Topic. They are summarized below.

- **Epigenetics** As one group put it, "we desperately need human epigenetics." There is presently a lack of knowledge of epigenetic processes, which may prove crucial in the interface between genes, environment, and disease. One group suggested that the National Toxicology Program should include the study of epigenetic change in its assays.
- **Genome maintenance/stability** Two groups felt that the study of DNA damage, repair, and maintenance is an important area of investigation, particularly with regard to aging, cancer, and cell death.

- **Signal transduction pathways** "Critical in understanding how the environment has effects on biological systems."
- **Developmental/Fetal Basis of Adult Disease** All groups recognized the importance of continuing and expanding research in this area, recommending further study of embryonic and fetal development (with that period's unique window of vulnerability to environmental insult), organogenesis, lung and neurological development, etc. This is a temporal issue involving transgenerational inheritance, and is particularly important for diabetes/obesity and infection/immune processes.
- **Aging** By the same token, several groups discussed the role of aging, both as another window of susceptibility/vulnerability, and as a study population of people affected or unaffected by diseases.
- **Oxidative stress/Inflammation** Continued recognition of the importance of this process, by which gene-environment interaction modulates disease onset, was discussed in some measure by all groups.
- **Stem cells** Mentioned in all groups, stem cell research received particular focus in one panel, which suggested that stem cells may represent an alternative to animal models in toxicology. The group also felt that stem cells could: (1) help determine how chemicals affect early differentiation, (2) help advance understanding of basic biology, (3) help understand disruption in biology, by contributing to cross-species comparisons with other developmental models such as C elegans and zebrafish, (4) help address the need for dose-response data, especially at low doses, and (5) help assess xenobiotic effects on blood/immune systems.

- **Immune system & Neurological system** Both of these systems, and their responses to challenge and/or disruption, were seen as important areas of discovery by some groups.

Proceedings of the NIEHS Strategic Planning Forum

October 17-18, 2005

Topic II:

Using Environmental Sciences and Environmental Exposures to Understand Human Diseases and Improve Human Health

- What will be the diseases and dysfunctions for which environmental exposures can best be used as a probe to enhance our understanding of their etiology?
- Which diseases and dysfunctions have a poorly understood etiology whose understanding would be enhanced most by studying the effects of environmental exposures? For which of these are the gaps in understanding disease pathogenesis greatest?
- What will be the diseases for which new understanding of environmental etiology would be most likely to lead to intervention and prevention strategies? Where can NIEHS have the greatest impact on public health?

E	F	G	H
John Peters	**Marschall Runge**	**Phil Iannaccone**	**Peyton Eggleston**
Dan Baden	Henry Falk	Marianne Berwick	George Daston
Deborah Brooks	Gwen Collman	John Essigmann	Shelia Zahm
Elaine Faustman	Lisa Greenhill	Marilie Gammon	Ruth Frischer
Jim Krieger	Michael Holsapple	Paul Lioy	Barbara Hulka
David Ozonoff	Fred Miller	Elise Miller	Fernando Martinez
Dhaval Patel	David Savitz	Isabelle Romieu	David Peden
Tom Sinks	Palmer Taylor	Cheryl Walker	Peter Spencer
Sholom Wacholder	Clarice Weinberg	Bruce Weir	Bill Suk
Allen Wilcox	Jerry Keusch		Nse Obot Witherspoon
			Darryl Zeldin
Susan Booker, writer	Liz Maull, writer	Kris Thayer, writer	Jerry Heindel, writer
Kimberly Thigpen Tart, recorder	Buck Grissom, recorder	Tom Hawkins, recorder	Ernie Hood, recorder

Overall, the groups struggled with efforts to answer the Topic questions with specific lists of diseases that should be studied, instead opting for the most part to produce general guidelines for consideration in a disease-oriented research direction. As will be described in more detail, one group distinctly disagreed with the tenor of the questions themselves, and implicitly with the disease-oriented direction in which they perceived the institute to be moving.

Some common themes did emerge, however, as did notable suggestions from individual groups.

Diseases of changing frequency or character

Participants felt most strongly that in order to use environmental exposures as a probe to enhance understanding of etiology, candidate diseases should stand out in specific ways. **High incidence** diseases, and **clusters** of disease, along with **low incidence diseases or clusters**, would be excellent targets for investigation of the role of environmental exposures in etiology, as would **unexplained increased or decreased occurrence** of diseases. One group expressed the idea in more global fashion, as diseases of "notably changing frequency or character," noting that it should be determined whether it is the nature of the disease itself or the diagnosis or reporting of the disease that is changing. Another panel noted that diseases whose **phenotypes** had **changed** in recent times would be ripe for study of the influence of environmental factors. **Intermediate phenotypes** and **intermediate outcomes** were also mentioned as potentially important targets to probe for environmental etiology.

Other epidemiological flags/Leveraging existing knowledge

One group suggested that **existing knowledge** could be leveraged to advantage in targeting diseases for study, including:

- Genetics (diseases where there are good genetic tools available)
- Environmental Factors (environmental influences on gene expression)
- Socioeconomic status
- Mechanisms
- Disease Burden
- Use existing resources such as CDC environmental exposure data

Another group expressed similar ideas, but suggested more specific criteria:

- Diseases with a strong **known genetic component** and **known environmental exposures**
- Diseases occurring in **stable populations**, and in **mobile populations**
- Diseases associated with **known receptor systems**
- **Comorbidity factors** (nutrition, infection, drugs, obesity, behavior) and disease
- Diseases with **developmental windows**
- Diseases associated with **specific exposures**

Another group, while noting that it is difficult to predict important disease-environmental exposure targets of opportunity due to the **bidirectional** nature of the **information flow** between diseases and exposures, did add notable ideas to the list of criteria for study of diseases:

- Diseases in which exposures leave an **imprint** (e.g., cancer, asthma, COPD, birth defects, immunological disorders)
- Diseases with the same **underlying mechanisms** (e.g., oxidative stress, inflammation)
- It should also be recognized that exposures can **exacerbate** as well as initiate a disease condition (e.g., lead)

The discussants were a bit more specific in their responses to Question #2, regarding poorly understood **etiology and gaps** in understanding disease pathogenesis, but still chose mainly to list overarching characteristics, exemplified by specific diseases or conditions:

- Diseases with some indication of **environmental role**, e.g., autoimmune diseases, autism, sexual development, obesity, reproductive diseases and disorders, neurodegenerative diseases, diabetes, cardiovascular diseases, pulmonary diseases
- **Chronic, long latency** diseases
- **Neurodevelopmental/neurodegenerative/neuropsychiatric** diseases, e.g., autism, ADHD, depression, schizophrenia, Alzheimer's, ALS, eating disorders
- **Distinct early development** diseases, e.g., autism, learning disabilities, birth defects, fetal basis of adult disease
- **Cancers** related to environmental exposures, e.g., prostate, breast, melanoma
- **Renal diseases** have been understudied in terms of environmental influences
- Diseases with **multiple and/or interactive risk factors**, e.g. those with infectious and environmental exposure components, and the potential immune/GI tract/nervous system interactions that may impact autism and learning disabilities

Knowledge gaps in understanding disease pathogenesis

One group's top concern was the potential health impacts of **emerging exposures** such as nanoparticles. **Mixtures**, and the importance of gaining understanding of real world combination exposures, was also mentioned, along with **multiple exposures, cumulative or aggregate**, arising from many sources, particularly the built environment. **Cultural and health disparities** were discussed, as was the need for better tracking of **disease clusters**. Gaining knowledge about the **positive influences** of the environment was considered important, which could yield both protective and risk factors. The need for improved **validity of animal models** was also discussed, with a desire for more communication among toxicologists, clinicians, and epidemiologists.

Question #3, which asked which diseases for which new understanding of environmental etiology would lead to intervention and prevention strategies, as well as where NIEHS could have the greatest impact on public health, engendered a diverse array of responses within the groups.

One group urged NIEHS to return to its early focus on the triad of pathogens, host, and environment. They felt that the most public health impact could be had in diseases where there has been a **changing pattern or incidence**, such as immune-mediated diseases, lupus, diabetes, asthma, and autism. Another group mentioned the known associations between **arsenic** and skin and liver cancer, and **mycotoxins** and liver cancer. A focus on important **existing and future exposures** was suggested as a route to high impact on public health, through measures such as **product reformulation** (e.g., alternate fuels), efforts to improve the **built environment** (e.g., use of alternative building products), promotion of the inclusion of **exposure measures** in electronic health rational databases, and expanded and more effective use of **new exposure measurement technologies** such as GIS and MEMS. The opportunity to improve **nutrition** was prominently mentioned, including the role of diet and dietary supplements, breastfeeding, the global search for natural dietary supplements, and the potential for low-calorie, low-fat diets to enhance longevity. Groups also discussed the need to conduct **research and interventions in populations of opportunity**, ranging from occupants of new buildings to victims of natural and unnatural acute exposures (e.g., 9/11, Hurricane Katrina), as well as larger populations of opportunity for the study of gene-environment interactions, based on ethnicity, lifestyle, cultural disparities, geography, etc. One group also felt that **individualized interventions** based on knowledge of SNPs and epigenetics would soon be of great value, along with the use of **siRNAs** to control genetic disease and impact the effects of environmental exposures.

As noted above, one group felt strongly that **the institute should maintain its present emphasis on exposure and basic science**, and that redirecting its efforts toward clinical interventions and disease-oriented research would ultimately compromise its effectiveness as a public health organization. The group embraced the integrative approach endorsed by the Topic #1 groups, but felt that it was critical that NIEHS retain its focus on exposure assessment, host susceptibility, and statistical analysis of gene-environment interactions. Selected excerpts from the group's PowerPoint presentation will further elaborate its position:

- The unique role of NIEHS is etiology and prevention, and this would have a broad focus on many diseases. Therefore, this unique orientation includes broad population-based approaches, looking at shared environmental factors and common mechanisms that underlie these diseases.
- We support NIEHS' broad mandate and continued interest in multiple disease processes.
- Embracing a broad, holistic, integrative approach to understand diseases is at the heart of the Institute mission. This means examining multilevel and multifactorial causality.
- We are not prepared to select single diseases. Instead, NIEHS should focus on environmental factors, especially those that are open to intervention and prevention.

- By doing exposure assessment, we can learn broad lessons to apply to multiple disease processes.
- NIEHS can have a great impact on public health by capitalizing on these common lessons learned and choosing diseases for their ability to elucidate shared exposures and mechanisms affecting either multiple health outcomes or single diseases of environmental etiology.

Proceedings of the NIEHS Strategic Planning Forum

October 17-18, 2005

Topic III:

Exposure Sciences: Needs, Opportunities, and Challenges

- What are the needs in environmental exposure assessment?
- What environmental exposures should we focus upon to have the greatest impact on human disease?
- What will be the emerging exposures of concern?
- What are the barriers to effective exposure assessment and toxicity assessment in humans?
- What technological or other innovations can improve our capacity in exposure and toxicity assessment?

A	B	C	D
Deborah Cory-Schlecta	**Hal Zenick**	**Martyn Smith**	**David Savitz**
Peyton Eggleston	Vas Aposhian	Mike Gallo	Dave Eaton
Bill Farland	Marianne Berwick	George Daston	Chris Bradfield
John Groopman	Elaine Faustman	Joe Graziano	John Essigmann
Lisa Greenhill	Bruce Hammock	Marilie Gammon	Bruce Lanphear
Irva Hertz-Picciotto	Michael Holsapple	Jim Krieger	Lee Newman
Elise Miller	Michelle Hooth	Dhaval Patel	Regina Santella
David Ozonoff	Tom Sinks	Marsha Wills-Karp	Fred Miller
Steve Safe	Nse Obot Witherspoon	Ellen Silbergeld	Shelia Zahm
Allen Wilcox		Jack Taylor	Barbara Hulka
Mary Wolfe, writer	Kim McAllister, writer	Pat Mastin, writer	Bill Jirles, writer
Janet Guthrie, recorder	Brenda Weis, recorder	Jerry Phelps, recorder	S. Holmgren, recorder

Unlike the previous breakout groups, these panels discussed and responded to the Topic questions sequentially, and their answers will be summarized in like fashion. A statement by one of the groups regarding the overall issue of exposure assessment is a pertinent introduction: “Exposure assessment is currently the Achilles heel of environmental health science. The methodology can often be weak, and often we tend to study things that lend themselves to measurement, such as persistent pesticides, even if they are not necessarily the most important thing to study."

Question #1:

- What are the needs in environmental exposure assessment?

Biomarkers

All groups identified a substantial need for more, improved, and validated biomarkers in exposure assessment. Two put that need at the top of their lists. Overall, a common desire for **validated biomarkers of exposure, susceptibility, and effect** was expressed; biomarkers that would be accurate for timeframes of interest (such as previous or historical exposures), are mechanistically linked to diseases of interest, and serve to link environmental exposures with effect. A need for a more comprehensive approach to biomarkers was identified. One group put this as a need for "multiple integrative markers;" another included a call for "identifying relationships among the biomarkers." These needs were identified within the context of discussion of the more global need for a more integrative approach to exposure assessment research itself.

Interdependent needs/Multiple applications

Each of the groups, in varying fashion, expressed a common interest in developing the **ability to conduct exposure assessment studies in a more comprehensive fashion**. One described the interdependent needs involved in any study—analytical methods, monitoring, modeling, as well as the ideal exposure measures, measures that would (1) be feasible to collect, (2) not be too expensive to collect or to assay, (3) would generate a reasonable statistical sample size, and (4) would measure something relevant to a disease process. Another group mentioned the need for collection of data at multiple levels in single studies, such as measuring biomarkers, personal monitoring data, and ambient air monitoring data, with the need for the weakest technology of these interdependent parts to still be strong enough to generate meaningful study results. Another wished for the ability to "measure many things simultaneously to discover new exposures, and then monitor a targeted list of things associated with a disease of interest," as well as the need for exposure data linking different phases of the exposure-disease continuum. This group made the point that effective environmental and disease intervention and prevention efforts could still be carried out while lacking complete information about the particular exposure-disease continuum, as good public health practice. They also called for "an integrated or coordinated effort to develop and apply exposure assessment approaches across agencies, institutes, and industry, in order to reduce costs and avoid duplication of effort." Similarly, another panel mentioned a need for standardized sampling methods and protocols.

Continued development of new exposure assessment technologies

All groups expressed support for the emerging new technologies within the field, and generally wished to see technologies that are “cheaper, faster, and better.” **Real time**, or **temporal measurement**, with quick turnaround, high throughput analysis of samples was seen as a hallmark, as were improvements in portability and sophistication of **personal monitoring (MEMS) devices**, **field monitoring and surveillance kits**, expanded use of **GIS technologies,** and the future value of **nanotechnology** for low-cost, micro-scale characterization of environmental samples. One group also discussed the need for **more accurate exposure questionnaires**, noting that few are standardized, validated, or correlate with biomarkers.

Other exposure assessment needs mentioned include:

- Researching high-level exposure opportunities, ubiquitous exposures, and low-dose dose-response.
- Clarification of pathways of exposure
- Validated measures of social environment
- Ability to assess exposures to admixtures, multiple complex exposures, and synergistic exposures
- Better understanding of bioavailability of toxicants

Question #2:

- What environmental exposures should we focus upon to have the greatest impact on human disease?

No clearly consistent patterns emerged from the group’s answers to this question. Therefore, a list of several of the bullet points from the groups’ presentations will be included.

- Fine particulates/ultrafine particles

  - air pollutants
  - indoor biomass burning
  - nanoparticles/nanomaterials
- Metals
- Solvents
- Pesticides
- Bio-aerosols (infectious agents, microbes, antigens, molds)
- Mycotoxins/fungal toxins
- Radioactive materials
- Tobacco
- Manganese
- Lead
- Diet (including “new dietary alternatives”)
- Interactions between micronutrients and environment
- Computer waste
- Replacement chemicals (pesticides, gasoline additives, etc.)
- Existing ubiquitous chemicals for which health information is lacking (e.g., PFOA, PDBE)
- Built environment exposures
- Pharmaceuticals in ground water/farm runoff

Some groups also included criteria for consideration of which environmental exposures to focus upon. These suggestions included:

- Persistent pollutants
- Widespread or increasing exposures
- Already known agents with adverse health effects
- Agents affecting common pathways/mechanisms with multiple endpoints
- Low level adverse exposures
- Disease of interest dictating exposures of interest
- Relative effects of cumulative, peak, and aggregate exposures
- Exposures associated with health disparities
- Decreasing rate of occupational exposures within the US

Question #3:

- What will be the emerging exposures of concern?

Similarly, groups compiled lists of emerging exposures of concern in answer to this question. They are consolidated below.

- Nanomaterials (mentioned by all four groups), ultrafine particles
- Climate change/global warming
- Pharmaceuticals, personal care products, bio-pharmaceuticals
- Global transmission of infectious and non-infectious agents/Emerging and re-emerging infectious diseases/Antibiotic resistant microbes/Microbial toxins
- Metals
- Industrialized food animal production/Aquaculture
- Existing ubiquitous chemicals
- Replacement chemicals
- New chemicals/new exposures, e.g. phthalates, bisphenol A
- Unknown exposures, e.g. Gulf War syndrome
- Fungal toxins
- Fluorinated compounds
- Water quality
- Food-related exposures

Question #4:

- What are the barriers to effective exposure assessment and toxicity assessment in humans?

Money and funding was the most consistently mentioned barrier. One group noted that "the current structure of the NIH study section tends to be unreceptive to applied research such as improving exposure assessment methodology; this situation must be changed if we are to meaningfully address exposure issues." The same panel cited the **cost of sampling** as a major barrier.

Ethical issues surrounding exposure assessment studies in human populations were also discussed by several groups. Confidentiality and IRB issues were mentioned as barriers to study, along with study subject results reporting requirements, even in the absence of interventional or therapeutic strategies. Along the same lines, difficulty in **identification of and access to appropriate exposed populations**, particularly high-risk populations such as ethnic and minority populations, was seen as a significant barrier, as were **access** to sample materials, reliable medical data, and bio-repositories.

The need for further **standardization and validation** in sampling methodologies, exposure assessment strategies and tools, and biomarkers and predictive models was also a common theme within the groups' discussions.

Limitations in relevance of data were another common theme, including a lack of information about the biological relevance of many exposures, particularly a lack of good temporal measures. One group also cited the need for better temporal and spatial congruence between environmental monitoring data, biomonitoring, and disease, as well as the difficulty of measuring cumulative exposure to mixtures, and an overall need for integrated measures of exposure assessment, including the omics technologies.

The **information overload** generated by large datasets was also mentioned. One group specifically cited the need for more access to and coordination of data generated through bioinformatics, biostatistics, and relational databases, requiring more specialists in these areas and an interdisciplinary team to interpret the data.

Other barriers identified by the groups included:

- Lack of clinical phenotypes
- Lack of suitably trained workforce
- Lack of availability of cost-effective and sensitive measurements of low-level exposures
- Difficulty linking existing exposure data with genetic susceptibility
- Need for microscale sample analyses

Question #5:

- What technological or other innovations can improve our capacity in exposure and toxicity assessment?

The groups featured a wide variety of answers to this question, in large measure reflecting several of the points made previously. The only area of innovation mentioned by all groups was **monitoring technologies**, including MEMS, real time personal and remote monitoring equipment, “smart dust,” and, although it is not monitoring as such, in the same vein, the groups all called for continued development and application of GIS, along with “the spatial statistics required to integrate GIS with environmental health science research needs.”

Discussants also returned to the issue of **biomarkers**. One group identified a need for several more specific biomarkers, particularly gene expression markers, single-cell sequencing of acquired mutations, methylation status of DNA, and the ability to link gene expression data with biomonitoring data. Another group suggested that it would be valuable to “focus on a specific exposure-disease relationship and address it using multiple exposure assessment tools. Need to develop multiple markers in the same study that can be integrated over space and time. Need to design the studies to collect the appropriate samples to answer the biological questions (some will be biomarkers of exposure, some of effect)."

Imaging technologies were also seen as a potentially rich area for innovation in EHS research, insofar as they can be used to identify functional changes in exposure and effects (e.g., MRI to quantify manganese and iron in the brain). Accelerator mass spectrometry as an ultra-sensitive way to detect exposures was mentioned, as was molecular imaging to investigate protein-protein interactions.

A variety of **improved analytical methods** was discussed. They included a call for growth in biorepository methods to make better use of (less) samples, as well as the need for improved methodology for uncertainty analysis in exposures, the development of better sampling algorithms, and advanced bioinformatics tools to integrate across disparate databases, such as to relate environmental exposure databases with existing health and disease databases.

Other needed innovations identified in the groups should be noted:

- Incorporation of **dietary information** in exposure assessment
- Development of **noninvasive techniques**
- More information about exposure and metabolism in **children and pregnant or lactating women**
- **Toxicokinetic** information and methodologies
- Continued development of **DNA adducts and protein adducts** as measures of biologically effective dose

- Continued development of **–omics** technologies to use as model systems to identify exposure/disease markers in human populations
- Community-based participatory research **(CBPR)**

Proceedings of the NIEHS Strategic Planning Forum

October 17-18, 2005

Topic IV:

Infrastructure Investment: Technological Needs and Applications

- What new technologies, tools, or approaches are needed for environmental health research? How can we promote innovation in basic, disease-oriented, and exposure-oriented research? How should we utilize new tools to have the greatest impact on our science?
- What investments in methodology/technology development represent the greatest needs for progress?
- Are there specific barriers to progress in technological innovation that NIEHS needs to be aware of?

E	F	G	H
Ken Ramos	**Kathleen Dixon**	**Jim Bus**	**Cheryl Walker**
Marschall Runge	Dan Baden	John Hildebrandt	John Peters
Trevor Archer	Phil Iannaccone	Deborah Cory-Slechta	Gwen Collman
Deborah Brooks	Robert Floyd	Traci Hall	Carol Henry
Cathy Koshland	Tom Kunkel	Ruth Frischer	Stephanie London
Fernando Martinez	Jerry Keusch	Cynthia McMurray	Carrie Redlich
Isabelle Romieu	David Peden	Peter Spencer	Bill Suk
Jim Popp	Ivan Rusyn	Randy Jirtle	Howard Hu
Paul Lioy	David Wheeler	Palmer Taylor	Bruce Weir
Clarice Weinberg		Sholom Wacholder	Darryl Zeldin
Susan Booker, writer	Liz Maull, writer	Kris Thayer, writer	Jerry Heindel, writer
Kimberly Thigpen Tart, recorder	Buck Grissom, recorder	Tom Hawkins, recorder	Ernie Hood, recorder

Each of the groups approached the Topic questions in a different manner. Therefore, this summary of their responses will be divided into two sections, the first enumerating responses regarding technology, the second concentrating on responses regarding the infrastructure of the research enterprise itself.

Technology

Of the many technologies, tools, or approaches addressed, only the need for improved **computational tools and bioinformatics** was discussed by all groups. In one group, this took the form of an emphasis on **mathematical models** and **data mining approaches** to understand biological systems and responses. Another noted that technologies and tools are available, but there is a lack of computational tools to take full advantage of them, particularly in the need for a **standardized tool for integration of computational toxicology data**. Another panel suggested the establishment of **bioinformatics centers** in the US, particularly in the fields of metabonomics and epigenetics. **Validation** of these methodologies and technologies is important to effectively manage, mine, and understand/interpret the huge amounts of data generated.

Most groups also mentioned the ongoing need for **high-end instrumentation** such as **imaging** and **high-throughput genotyping**. It was suggested that NIEHS foster efforts to **coordinate and collaborate** in the use of such expensive instruments, such as consortia among researchers and universities to improve and expand access to equipment. One group gave high priority to improvements in imaging technologies, calling for (1) new probes that will report out specific processes applied to environmental agents, (2) technologies to monitor tissue-, cell-, and organism-specific effects within the context of the tissue, and (3) tools to follow conformational changes within multiprotein pathways. Similarly, another group identified a need for imaging studies at the subcellular, tissue, animal, and population levels, while another asked more generically for technologies that make measures at the level of the single cell. A group also recommended investment in resource-intensive mass spectrometry and NMR for use in metabonomics and proteomics research, to help develop and validate biomarkers. One group also identified a barrier to deployment of high-end instrumentation, noting that grants to purchase such equipment exist, but fail to provide support sufficient to achieve self-sustaining status.

As has been seen with other Topics, the need for continuing investment in the discovery, development, and validation of **biomarkers** was also a common theme within these discussion groups. **Non-invasive** biomarkers, biomarkers that measure **pre-disease** status, and **intermediate** biomarkers of disease were specifically mentioned. One group called for long-term study of **small cohorts** to include assessment of biomarkers over time.

Several groups discussed the need for **more sophisticated exposure assessment methods and tools**. They need to be **more sensitive**, and able to measure **personal and cumulative exposures**. Nutrition should be included as a metric. One group also mentioned a need for tools that will measure **near range** exposures, and **dispersion of agents** through the environment. Groups also suggested further investment in refinement and validation of **animal models** as tools to assist in exposure assessment by modeling environmentally relevant doses and relevant pathways of exposure, approximating human exposures and responses. One panel called for the development of whole animal tissue specific **siRNA laboratories** as a faster and cheaper adjunct to transgenic models.

Other technological/methodological infrastructure needs mentioned included:

- Better tools to understand **social aspects/inequities**
- Willingness to invest in infrastructure needed to conduct **epidemiologic studies**
- **Databases, repositories, and registries** require stability in administration, funding, and access. NIEHS should partner or lead in such efforts.
- Simple, economical methods for **field study**
- Better **GIS/GPS sensors** to detect multiple (vs. single) agents
- Economical, deployable, **real-time sampling methods** for environmental and personal monitoring
- More and better **access to appropriate populations** through twin registries, occupational cohorts, etc.

Research Enterprise Infrastructure

Points were raised regarding the research enterprise infrastructure mainly, but not exclusively, in response to Question #3, which asked for identification of barriers to technological progress.

The major barriers alluded to within the discussions were the need to encourage and support **cross-disciplinary and multidisciplinary research**, and infrastructural impediments to **innovative, high-risk research**. In some cases, both barriers were entwined within a group's response. For example, one group recommended that the research enterprise "unlock the system; stress innovation in a peer review process. Find a place for high-risk, innovative, multidisciplinary research." The same group identified specific barriers that discourage cross-disciplinary research and innovation: (1) training modalities, (2) funding mechanisms, (3) study section membership, and (4) current reward systems.

Within the context of multidisciplinary research, several groups mentioned a need to encourage innovation and high-risk research through the establishment of **non-traditional teams**, including, for example, engineers and materials scientists along with EHS researchers. It was suggested that EHS could look to other fields and institutions (e.g., DARPA) for prototypes of such teams, which should be goal-oriented, organized to work backward from a specified goal.

Similarly, groups identified **funding mechanisms as a barrier** to collaboration and innovation to foster technological and methodological progress. Of particular note, two groups focused on the current structural tendency to favor funding of investigator-initiated, single investigator research as a significant barrier to team approaches, resulting in a linear (vs. parallel) research direction. One group suggested "investment in new vehicles to fulfill needs not met via investigator-initiated research (e.g., comparison and validation of existing biomarkers), with an emphasis on hypothesis-directed experiments vs. hypothesis-generating research." Another group noted that no funding mechanisms exist to foster collaborative projects between the engineering and science communities, and suggested that there are some such mechanisms within NSF that could be emulated. The same group mentioned that (1) cores outside of the Center mechanism do not exist, (2) the field should move toward Program Announcements and away from RFAs, and (3) "Glue Grants," which mandate collaboration between institutions with complementary skills, should be considered.[*]

[*] This collaborative research program sponsored by NIGMS is a new mechanism that encourages independently-funded investigators to work together to solve a major biomedical research problem. The funds are intended to provide the "glue" to bring investigators together and allow them to work together interactively. The program also provides unique opportunities to attract the expertise of other scientists who have not traditionally been involved in biomedical research, such as engineers and informatics specialists.

Other infrastructure needs worthy of note included:

- Providing infrastructure for study of **large cohorts**
- A need for **comparative studies** between high and low exposure populations
- **Technology transfer**, under the Bayh-Dole Act, has caused limited access to research results and an inhibition of scientific knowledge dissemination

Proceedings of the NIEHS Strategic Planning Forum

October 17-18, 2005

Topic V:

Global Health: Environmental Health Priorities & Opportunities

- What will be the key research opportunities globally, both for understanding environmental etiology of human disease as well as to develop and test interventions? What is the best way to identify the opportunities with the greatest potential impact?
- What are the barriers to global partnerships to conduct environmental health research?

A	B	C	D
John Groopman	**Joe Graziano**	**John Essigman**	**Dan Baden**
Traci Hall	Jim Bus	John Peters	Vas Aposhian
Martyn Smith	Gwen Collman	Ellen Silbergeld	Tom Sinks
David Ozonoff	Cynthia McMurray	Jim Popp	Jim Swenberg
Marsha Wills-Karp	Bill Farland	Allen Wilcox	Jerry Keusch
Paul Lioy	Tom Kunkel	Carol Henry	Dave Eaton
George Daston	Elise Miller	Hal Zenick	Bruce Hammock
Peter Spencer	Shelia Zahm	Stephanie London	Marilie Gammon
	Ruth Frischer	Isabelle Romieu	Peyton Eggleston
		Nse Obot Witherspoon	Bill Suk
Mary Wolfe, writer	Kim McAllister, writer	Pat Mastin, writer	Bill Jirles, writer
Janet Guthrie, recorder	Brenda Weis, recorder	Jerry Phelps, recorder	S. Holmgren, recorder

As was the case with some of the prior Topics, the groups' discussions of this Topic were wide-ranging, and did not fall into a pattern of discrete answers to the questions posed. Therefore, the summary of their deliberations will address the major concerns that arose, and delineate the many responses of interest.

In terms of identified global opportunities for research and intervention, three areas achieved consensus, having been discussed by all groups.

Climate change/Global warming

Groups felt that it will be important to assess the **biological and health effects** of global warming. These could include increases in vector-borne diseases, infectious diseases, heat-related adverse effects, fungal changes, algae blooms, and the appearance of known toxins in new species. There was concern about "who owns this issue (e.g., NIEHS, NIAID, Fogarty)." Also, group noted that it will be necessary to "address the structural funding barriers engendered by the global problems of climate change."

Globalization of pollution and hazardous substances

All groups expressed concern about these dangers, particularly in terms of **migration of pollution** to the US from foreign source points, and generally across geographic boundaries, regardless of final destination. **Mercury** and pollutants generated by the burning of **coal** were particularly worrisome. Along similar lines, one group mentioned "intercontinental transports" of hazardous substances, inadvertent transports (e.g., ballast, airliner air), and transport of infectious diseases or vectors.

Urbanization

Several groups also felt that the **global trend toward urbanization**, with the establishment of "mega-cities" and rapid change from rural to urban economies, is a good candidate for research and intervention strategies. **Built environment** issues will soon affect two-thirds of the world's population. One group suggested that NIEHS, with its pioneering role in studying the health effects of the built environment, consider partnering with NIMH or NICHD on this issue.

Other research and intervention needs/opportunities fell into three general categories. None of the individual responses within those categories approached consensus, so they will be listed to show the breadth of concerns within the community.

Specific problems

- **Arctic regions**: persistent organic pollutants
- **Coastal** and **ocean** issues
- **Occupational exposures**: compare earlier US industrial exposures with those being experienced in developing countries
- **Indoor combustion of biomass**
- **Arsenic**
- **Food supply contamination** – e.g., pesticides, microbial
- **Natural disasters** – opportunity for research and interventions in populations with high exposures
- **Computer waste** – e.g., metals, solvents
- **Diseases of interest** per global disease burden
  - Infectious
  - Cardiovascular
  - Respiratory
  - Cancer
  - Neurological
- **Agents of interest**
  - Air pollution
  - Mycotoxins
  - Smoking
  - Occupations
  - Food products
  - Diet
  - Metals
  - Sunlight
  - Pesticides

Research approaches/opportunities

- Study **pockets of health and/or longevity**
- **Compare** US immigrants to native populations
- **Compare** diseases between US and foreign populations to identify differences in lifestyles and exposures
- Identify **foci** of exposures (e.g., biomass burning, air pollution)
- Track emerging **"diseases of affluence"** in developing countries
- Assess health consequences of **rural poverty** and associated exposures; impact of diet and nutrition interventions
- Target **maternal/child health**
- Study **variations in populations** (e.g., African vs. western populations)
- Study **exposed populations** and develop **interventions appropriate** to the population

Policy/initiative/resource ideas

- **Long-term interventions** should be developed, and supported even after a study is completed. Groups were concerned about the **funding sustainability** of such programs.
- Identify areas with **unique data opportunities**, such as standardized medical record-keeping, or countries with established disease registries. In western countries with sophisticated medical records, consider **combining studies** around a single research question, e.g. PM
- Conduct research in countries where optimal benefits can be realized due to rapid **translation of findings into policy**. Directly involve Ministries of Health in studies.
- Search for **natural, pharmacological, and nutritional agents** that reverse biomarkers associated with disease outcomes
- Focus on countries and diseases with a **high burden** of exposure, number affected, and a health outcome of concern.
- **Apply new exposure assessment technologies** to address research questions in global population studies.

In each of the groups, there was a great deal of discussion about **partnerships** as vehicles for expanding opportunities for global research, collaboration, cooperation, and intervention. Conceptually, discussants agreed that it is vital that global partnerships must foster **trust, honesty, and mutual benefit**. Noting that “fundamentally, public health is global health,” one group summarized this need succinctly: “Successful global health research can only be done when both parties respect the other’s needs, and when the partnerships are equal and benefits of the research accrue both to the researchers and the study population. Ideally, studies would leverage the strengths of both partners.”

The vital importance of **cultural sensitivity** in global partnerships was also emphasized. It can help to partner with organizations that have access to and cultural knowledge of a particular area. Also, cultural facets such as payment mechanisms, linguistics, religious traditions, health and disease beliefs, and gender roles should be taken into account when entering into partnerships and designing studies and intervention strategies, and should be communicated to the researchers involved.

<u>Partnership suggestions</u>

Groups came up with a wide variety of ideas about how NIEHS could successfully engage in partnerships to conduct global EHS research and interventions. One theme that emerged was that NIEHS should “lead with its strengths” in basic research, epidemiology, exposure assessment, and toxicology, leveraging those areas of expertise to **connect with existing organizations and programs**—partnering with existing cohorts, networks, and programs (e.g., Gates Foundation AIDS and malaria research). One group suggested that NIEHS strategize with other national and international agencies already involved with environmental health initiatives, such as EPA, WHO, and PANO. Another advocated the formation of a consortium, suggesting CDC, WHO, Gates Foundation, Soros Foundation, Fogarty Foundation, foreign universities and research labs, governments in other developed countries, and other NIH institutes as potential members of such an enterprise. It was also noted among the groups that NIEHS should consider partnering with public health organizations in developing countries to provide traditional public health interventions, such as safe drinking water. NIEHS is also encouraged to provide opportunities for EHS education internationally, including teaching fellowships and children's education programs.

Several other specific suggestions were offered on ways for NIEHS to promote and conduct global EHS research and intervention through collaborations and new initiatives:

- Work with universities to develop **regional environmental health centers** designed to work in collaboration with NGOs and governments
- Encourage NIEHS centers and SBRP to have **international partners**, a la the "Sister Cities" program
- Build on experiences and expertise gained through Fogarty's International Training in Environmental and Occupational Health **(ITREOH) program**
- NIEHS should support opportunities for **peer networking**, such as funding scientists from developing countries to attend international

meetings, and funding US scientists to attend Fogarty network meetings

- NIEHS should hold a **meeting to address infrastructural barriers** to the ability to conduct efficient, effective global EHS research and interventions
- An **IRG** is needed for EHS. It should have a study section devoted to global EHS, with a **special emphasis panel at NIEHS**.

Barriers

Groups identified and discussed many potential barriers to successful pursuit of global EHS efforts. They can be roughly categorized as conceptual barriers, barriers in practice, and agency/funding barriers.

Conceptual barriers

Several groups mentioned the problem of **conflicting objectives or contradictory goals** when working with international partners. For example, there can be an inherent conflict between the pursuit of research opportunities and the implementation of public health interventions. Research partners may have conflicting aims, and different mandates that may be overlapping. The potential for **duplication of efforts** was also mentioned as a possible barrier to success.

A **need for trained personnel** and a **lack of medical care infrastructure** in countries of interest were seen to be barriers. Groups mentioned a need for capacity building, with locally trained people available to understand the issues and do the work on local problems.

One group also expressed concern that "failure to recognize/include/learn about **culture-specific knowledge** in research design and execution can severely limit both the quality of the research and our ability to recruit collaborators and study subjects."

Barriers in practice

- Lack of good, validated environmental **exposure tools** appropriate to multicultural settings
- Lack of expertise and granting mechanisms to couple **computer technology** with EHS
- **Post-9/11 issues**—disincentives for foreign students to attend US universities affects our ability to develop future potential collaborations
- **Political stability/civil unrest**
- **Governmental priorities** in countries of research and their willingness to take action
- **Language** barriers
- International **sample transfer** and **intellectual property** issues

Agency/funding barriers

One group noted that the **current NIEHS structure** does not readily allow for funding global issues. Similarly, in terms of research relevance, another group mentioned that **NIH policy** is unclear about whether the research goals of an application need to address questions that cannot be addressed in the US, but are important to NIH. Two groups noted that NIH only provides 8% of overhead for foreign grants. As one group put it, that "does not cover much, and makes it difficult to develop foreign partnerships at this funding level…it creates the appearance that we are not making them a direct partner if we cannot support their indirect costs." Another group suggested that granting agencies need to adopt more realistic, **longer-term grant periods**, in that it is "ambitious to believe that a program will be productive with a 3-5-year window." **Fiscal management** was also seen as a barrier, both in terms of "care and feeding of the partnership (what is NIEHS' role?)", and the possibility of an absence of sound fiscal management in other countries.

Topic VI:

Training in Environmental Health Sciences: Pipeline, Content, and Future

- How do we attract the best and brightest individuals to environmental health research?
- What should our training goals be?
- How can we attract more physician-scientists to environmental health sciences?
- What are the key disciplines for which interdisciplinary training opportunities need to be enhanced? Where can NIEHS have the greatest impact?
- What are the barriers to effective interdisciplinary research and training? What can NIEHS do to help overcome these barriers?
- What are the most innovative ways NIEHS can "grow" future researchers in environmental health sciences?

E	F	G	H
Ken Ramos	**Kathleen Dixon**	**Jim Bus**	**Cheryl Walker**
Marschall Runge	Dan Baden	John Hildebrandt	John Peters
Trevor Archer	Phil Iannaccone	Deborah Cory-Slechta	Gwen Collman
Deborah Brooks	Robert Floyd	Traci Hall	Carol Henry
Cathy Koshland	Tom Kunkel	Ruth Frischer	Stephanie London
Fernando Martinez	Jerry Keusch	Cynthia McMurray	Carrie Redlich
Isabelle Romieu	David Peden	Peter Spencer	Bill Suk
Jim Popp	Ivan Rusyn	Randy Jirtle	Howard Hu
Paul Lioy	David Wheeler	Palmer Taylor	Bruce Weir
Clarice Weinberg		Sholom Wacholder	Darryl Zeldin
Susan Booker, writer	Liz Maull, writer	Kris Thayer, writer	Jerry Heindel, writer
Kimberly Thigpen Tart, recorder	Buck Grissom, recorder	Tom Hawkins, recorder	Ernie Hood, recorder

In the groups' discussions of this Topic, for the most part the questions were dealt with in order. There were a great many ideas and suggestions posited, some of which fell into general categories, while others were quite specific.

Question #1:

- How do we attract the best and brightest individuals to environmental health research?

K-12 & undergraduate programs

The inclusion of EHS in K-12 (particularly middle and high schools) and undergraduate programs was emphasized in all groups as perhaps the most promising method of attracting the best and brightest to environmental health research. One group specifically felt that **NIEHS should reinstate its K-12 Centers program**. Another suggested leveraging with other partners to **establish K-12 programs**, targeting teachers and advisors, and using environmental issues as a "hook" to interest young people in the field. The field should also be presented at those levels as an **attractive, diverse career option** with ample funding opportunities and attractive salaries, as well as a **rewarding career** with the opportunity to make a difference in the community.

All groups recognized a need to **expand EHS information and opportunities at the undergraduate level**. **Attractive courses in EHS** should be included in the undergraduate curriculum, such as seminar courses to showcase EHS as an interdisciplinary science. **Undergraduate training and research programs** in EHS should also be supported to attract bright students and make them aware of the avenues to further education in the field. For example, existing mechanisms for undergraduate training and research could be tapped into, with undergraduate majors applying to programs designed to provide research experience—in this scenario, students would be jointly paid by PIs and the university. **PIs** should be stimulated to develop programs for undergraduates, including **seminars and laboratory experiences**. Similarly, SBRP and centers, and any university with a significant number of EHS grantees should be encouraged to include undergraduates in their activities. One group noted that **undergraduate research programs and internships** such as summer programs "have made a huge difference in decisions to go forward with advanced education." It is important that early in their education students be made aware of the **viability of EHS as a career**, and of the **cross-disciplinary** nature of the field.

Graduate & Postgraduate-level programs

Enhanced support for training grants received much attention, with one group calling for 100% tuition training grants. Groups also mentioned the need to **retain EHS trainees** within the field, persuading students to stay in academia rather than migrate to industry. One suggestion to accomplish that was to **increase funding for young investigators**, to keep them interested in the field and supported. Another noted that **double degree options** have been enormously productive for research, also pointing out that providing **research fellowships for MPH students** increases the field's competitiveness for faculty positions. There is a need for **coordinated mentoring programs**, helping mentor students along EHS career paths. Also, **pride in the field** needs to be encouraged, which will help reverse its sometimes negative image as an applied science. Another group mentioned the ongoing need to **recruit international students**.

Several other suggestions on how to attract the best and brightest to the field that arose during the discussions should be noted:

- **Field experiences** bring the field alive
- **Awards and prizes**
- **Increased likelihood of funding** via (1) review sections that recognize environmental health, (2) continuing to offer center grants with stable, long-term funding, and (3) increasing program project grants
- A general need to **better define and market EHS**, e.g., by advertising at career fairs and (NIEHS) working with the broader community, such as industry and professional societies
- **Career development** in EHS should be thought of as a continuum, with entrance points at the undergraduate, graduate, and postgraduate levels. As a specialized field, the decision to pursue EHS is likely to occur later in the education process, however, **customized approaches** should be developed to attract the different disciplines needed within the field, at different points in the pipeline.

Question #2:

- What should our training goals be?

The groups' answers to this question covered much of the same territory as Question #1. Interestingly, while two groups emphasized a strong need for **discipline-based training**—"solid undergraduate training in a specific discipline as a foundation for later interdisciplinary training"—the others chose to focus on a need to provide **interdisciplinary training opportunities**, in collaboration with fields such as bioinformatics, engineering, and social work. As one group expressed, "Be sure we cover the breadth of EHS, extending from epidemiology through basic laboratory science to clinical sciences…train interdisciplinary scientists."

There was further call to develop environmental health training programs at the undergraduate and graduate levels, including "earn while you learn" programs for promising undergraduates, MDs, and DVMs, as well as undergraduate programs with sufficient salaries, and loan forgiveness programs. One group added that it is important to emphasize the hypothesis-testing, troubleshooting, and dynamic aspects of science during K-12 education.

Another group listed the **subject areas** within the field that should be focused upon in training endeavors:

- Basic physiology
- Statistics
- Epidemiology
- Biostatistics
- Anatomy
- Other basics critical to integration
- Knowledge of gene-environment interactions
- Knowledge of biomarkers
- Population-level approaches
- Ecology
- Intervention studies/approaches

Question #3:

- How can we attract more physician-scientists to environmental health sciences?

Much of the discussion regarding this question centered on medical school programs. It was felt to be particularly important to work to **incorporate EHS into medical school curricula**, which is presently often not the case. It was suggested that NIEHS partner with other institutes to **develop fellowships in environmental medicine**, which would relate directly to the institute's disease focus. Also, **summer EHS training programs for medical students** were endorsed, as was the development of **grand rounds seminars** in EHS for use across the nation, which could be produced without large training grants.

Aside from medical school initiatives, several other actions were suggested to attract more physician-scientists to EHS, including:

- Grants programs to **attract practitioners mid-career**, as clinicians see the importance of increasing their knowledge of environmental aspects of their practices
- Establish a **certification mechanism** to provide a defined set of skills as the end product (e.g., board subspecialty)
- Offer **additional master's-level degrees**
- **Evaluate current training practices** to see how EHS could be better incorporated
- Strengthen the number of **MD/PhD programs** with EHS training
- Offer **seminars at society meetings** to attract interest in EHS
- Offer **residencies in occupational and environmental medicine**, with an increased emphasis on the environmental component, perhaps in conjunction with NIOSH
- NIEHS should take the lead in developing **clinical programs** that would attract clinicians

Question #4:

- What are the key disciplines for which interdisciplinary training opportunities need to be enhanced? Where can NIEHS have the greatest impact?

Groups mainly responded to this question in the form of a list of key disciplines, which is compiled below.

There was consensus among the groups that it is vital to enhance interdisciplinary training opportunities among: biostatistics, bioinformatics, environmental and bioengineering, exposure, toxicology, and genetics.

Other disciplines mentioned included:

- Endocrinology
- Physiology
- Risk Assessment
- Surveillance Techniques
- Biomedical
- Pathology
- Pharmacology
- Clinical Sciences
- Epidemiology
- Ecology

One group also suggested that occupational medicine be offered as an elective at medical schools, that cross training with public health should occur, and that there should be increased quantitative training in biological sciences.

Question #5:

- What are the barriers to effective interdisciplinary research and training? What can NIEHS do to help overcome these barriers?

Many salient points were raised during discussions of this question. However, none were mentioned by more than a single group. Therefore, responses will be listed, divided into the barriers identified, and recommended actions or solutions.

Barriers to interdisciplinary research and training

- **Center grants**: demanding only those with EHS funding or only MDs thwarts interdisciplinary research
- **RO1 mechanism** allows only one PI
- **Tension** between depth and breadth of training
- **Cross-disciplinary training grants** layer on extra requirements that are difficult to complete
- **Funding**
- Difficult to get **credit** for interdisciplinary work
- **Current promotion and tenure criteria** do not generally give credit for collaborative research
- **Have not promoted skills** to work in collaborative situations

Recommended actions/solutions

- Encourage **cross-disciplinary appreciation** of the skills brought to the table
- NIEHS has made some progress in encouraging inclusion of multiple disciplines
- Recognize **benefits of co-investigators**, in allowing career development of individual members in a research team
- **Recognize all authors** in collaborative publications
- Create **additional EHS training grants**
- Give higher priority for funding to grants that **identify assistant professors** in collaborative research
- Allow **co-principal investigator grants**
- Revamp **promotion and tenure criteria**
- Stimulate addition of EHS into **medical school curricula**
- Stimulate **interdisciplinary training programs**
    - o Refocus NIEHS training programs
    - o Base renewals on interdisciplinary focus and success
- Encourage **dual mentorship** for graduate and post-doctoral students
    - o Interdisciplinary training emphasized
    - o Develop grant program to stimulate dual mentors

- Make interdisciplinary training part of **SBRP and Centers** programs
- Work to **decrease "silo effect"** in environmental sciences
- Bring in **more stakeholders** to work together to develop partnerships

Question #6:

- What are the most innovative ways NIEHS can "grow" future researchers in environmental health sciences?

Again, responses to this question were widely varied, with none mentioned in more than a single group.

- Establish **partnerships with corporations and foundations** to expand the funding base, e.g., Google, Fogarty, Burroughs Wellcome Fund, US Mexico Foundation, Gates Foundation
- Create an effective international strategy by **partnering with other countries** to stimulate interest in EHS
- Give people a sense of belonging to an **elite, new, exciting field**
- Establish a **greater presence at meetings**
    - Fund sessions at multiple relevant specialty meetings
    - Sponsor symposia focused on environmental health
- **Journals**
    - Environmental health sections in established journals
    - Editorials, review articles
    - EHP as an outlet for research and views
    - Local newspapers
- Make **T32 programs** recognize integration
- **Loan forgiveness** programs
- Establish an **"AmeriCorps/ROTC"** type of program for NIEHS
- **Use media** to develop the pipeline (e.g., cartoons targeted at children.